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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/331,375	12/03/1999	CHARLES M. COHEN	CIBT-P01-519	1578

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EXAMINER
DEBERRY, REGINA M

ART UNIT	PAPER NUMBER
1647	13

DATE MAILED: 05/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/331,375	COHEN ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *2-4,21-23,25-27 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-20,24,28 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-30* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

Status of Application, Amendments and/or Claims

The information disclosure statement filed 08 January 2002 (Paper No. 11) was received and complies with the provisions of 37 CFR §§1.97 and 1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits.

The amendment filed 16 January 2002 (Paper No. 12) has been entered in full. Applicant's election of Group I (claims 1, 5-20, 24, 28 and 29) with traverse in Paper No. 12 is acknowledged. The traversal is on the grounds that there is no evidence that the morphogen, inducers, agonists and activators are classified in different art groups, and that relevant prior art to any of these compositions cannot be found in an art location which does not include any of the other compositions. Contrary to Applicant's assertion, the inventions recite different compositions. Small molecule morphogenic activators and inducers and agonists of morphogens can encompass proteins, nucleic acid and chemicals. These compositions would be classified and found in different art locations. The requirement is still deemed proper and is therefore made FINAL. Claims 2-4, 21-23, 25-27 and 30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12.

Priority

A claim to priority under 35 USC 371 must contain a specific reference to such in the first paragraph of the first page of the specification.

Furthermore, if applicant desires priority under 35 U.S.C. 119(e) based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph.

If the application is a utility or plant application filed on or after November 29, 2000, any claim for priority must be made during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2) and (a)(5). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) a surcharge under 37 CFR 1.17(t), and (2) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Commissioner may require additional information where there is a question whether the delay was unintentional. The petition should be directed to the Office of Petitions, Box DAC, Assistant Commissioner for Patents, Washington, DC 20231.

Abstract

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Specification

The disclosure is objected to because of the following informalities: In the Brief Description of the Figures (page 10, lines 21), Figure 1 states "panels 1-1 through 1-12" but the drawing are listed as "Fig. 1A-1L". Appropriate correction is required.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,5, 8-10, 15, 16, 20, 24, 28 and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Field, WO 95/14079 (IDS # AA, Paper No. 11).

Field teaches a method of implanting a preparation of skeletal myoblasts into myocardial tissues of animals (page 3, lines 16-20 and page 7, lines 12-23). It is noted that all animals are at risk of loss or damage to the myocardium. Field teaches that the grafts can be proliferative (page 9, lines 15-23). Grafts of the invention are useful to replace diseased or damaged tissue to supplement myocardial function. The graft that is transplanted into myocardial tissues of animals can express morphogens and thus the grafted cells are treated with morphogens during and after implantation (page 9, line 31-page 10, lines 1-11).

Field teaches cultured skeletal myoblast (C2C12) in 20% fetal bovine serum (page 16, lines 15-19). The specification states that myogenic precursor cells are variously referred to in the literature as myoblast, muscle stem cells or satellite cells (see specification, page 11, lines 16-20) and thus Field's skeletal myoblast cells meet the limitation "myogenic precursor cells" recited in the claims. The specification defines morphogens (growth factors) as proteins regulating cell proliferation and/or differentiation (see specification page 3, lines 23-25). Fetal calf serum and fetal bovine serum contain growth factors such as insulin growth factor (soluble forms of morphogens), thus meeting the limitation of cells being treated with morphogens before implantation as recited in the claims (for review please see attachments on fetal calf serum and fetal bovine serum). Field teaches proliferation and the differentiation of cultured skeletal myoblast using 2% horse serum (page 16, lines 21-24 and page 17, lines 13-28). Cultured myoblast were injected into the myocardium of mice. Differentiated cells were observed in hearts receiving myoblast injections (page 17, line 29-page 18, line 19). Field teaches a method of inducing myoblast to differentiate into cardiomyocytes and DNA synthesis in vascular endothelial cells via delivery of a morphogen (page 30-32). A fusion gene comprising TGF-β1 (morphogen) was transfected into C2C12 myoblasts (page 29, lines 23-27). Myoblasts carrying the TGF-β1 gene were used to produce intra-cardiac graft in mice.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6, 7, 11, 12, 13,14, 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Field, WO 95/14079 (IDS # AA, Paper No. 11) in view of Cohen *et al.* WO 92/15323. The teachings of Field are discussed above in the 102(b) rejection. Field does not teach a method of treating specific heart conditions, autologous skeletal muscle satellite cells, treatment steps, concentrations of morphogens, osteogenic and bone morphogenic proteins.

Cohen *et al.* WO 92/15323 teach administration of morphogen-treated cells which are useful in the replacement of diseased or damaged tissue in a mammal (see page 7, lines 12-25). The morphogenic activity includes the ability to induce

proliferation and differentiation of uncommitted progenitor cells (page 6, lines 1-12). The genus of uncommitted progenitor cells would include the species of myogenic precursor cells, including autologous skeletal muscle cells (page 60, line 33-page 61, line 9 and page 44, line 4). The invention may be useful in the repair of damaged heart or blood vessel tissue as may result from cardiomyopathies and/or atherothrombotic or cardioembolic strokes (page 6, lines 26-page 7, lines 10). Cohen teaches cell stimulated *ex vivo* by contact with proteins or agents capable of stimulating morphogen expression in these cells also may be provided to the tissue locus. The morphogens may be used to increase or regenerate a progenitor or stem cell population in a mammal. Progenitor cells, for example, may be isolated from an individual's bone marrow stimulated *ex vivo* for a time at a morphogen concentration sufficient to induce the cells to proliferate, and returned to the bone marrow. Cells may be stimulated in culture and provided to the body (page 8, lines 7-30). Cohen states that progenitor cells may be stimulated *ex vivo* by contacting progenitor cells of the population to be enhanced with a morphogen under sterile conditions at a concentration and for a time sufficient to stimulate proliferation of the cells. The stimulated cells then are provided to the individual as, for example, by injecting the cells to an appropriated *in vivo* locus. This would include autologous skeletal muscle satellite cells (page 60, line 33-page 61, line 9 and page 44, line 4).

Cohen teaches OP-1, OP-2 and CBMP-2 proteins (page 11, lines 13-15, page 43, lines 21-30 and page 44, lines 16-32). Cohen teaches purified recombinant human OP-1, mature form (page 63, lines 6-15). A sterile biocompatible composition containing morphogen-stimulated progenitor cells may be provided to the tissue locus

(page 61, lines 19-30). Cohen teaches the differentiation and proliferation of cultured cells in the presence of a morphogen (page 55, lines 20-page 56, line 19 and page 59, lines 16-26). Cohen teaches morphogen concentrations which overlap the instant concentrations (page 56, lines 18-33).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Field regarding methods of transplanting morphogen-treated myogenic precursor cells into damage myocardium by using the teachings of Cohen regarding specific morphogenetic proteins, specific heart conditions, autologous skeletal muscle satellite cells and morphogen concentrations. The motivation and expected success is provided by both Field and Cohen who teach that a morphogen can be expressed in progenitor cells and transplanted into tissue and Cohen who teaches the properties of various morphogens regarding proliferation and differentiation. Furthermore, one of ordinary skill in the art of developing a method for treatment would be motivated to include adjustments of working conditions such as varying treatment steps because these adjustments are deemed a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (703) 305-6915. The examiner can normally be reached on Mondays-Fridays 8:00 a.m. - 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

RMD

ELIZABETH KEMMERER
PRIMARY EXAMINER

RMD
April 29, 2002